Systemic Lupus and Cardiovascular Disease

A Brief Overview

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ACR Criteria for Lupus*

- Malar Rash
- Discoid Rash
- Photosensitivity
- Oral Ulcers
- Arthritis
- Serositis (pericard.-pleura)
- Renal Disorder: (eg proteinuria)
- Neuro Disorder: (seizures/psychosis)
- Heme Disorder: (low platelets, etc)
- Immunologic Disorder (AntiDS DNA; Anti Sm; APL Ab)
- + Antinuclear Ab (ANA)

4 required to include in SLE cohort

* These are NOT Diagnostic Criteria

Lupus

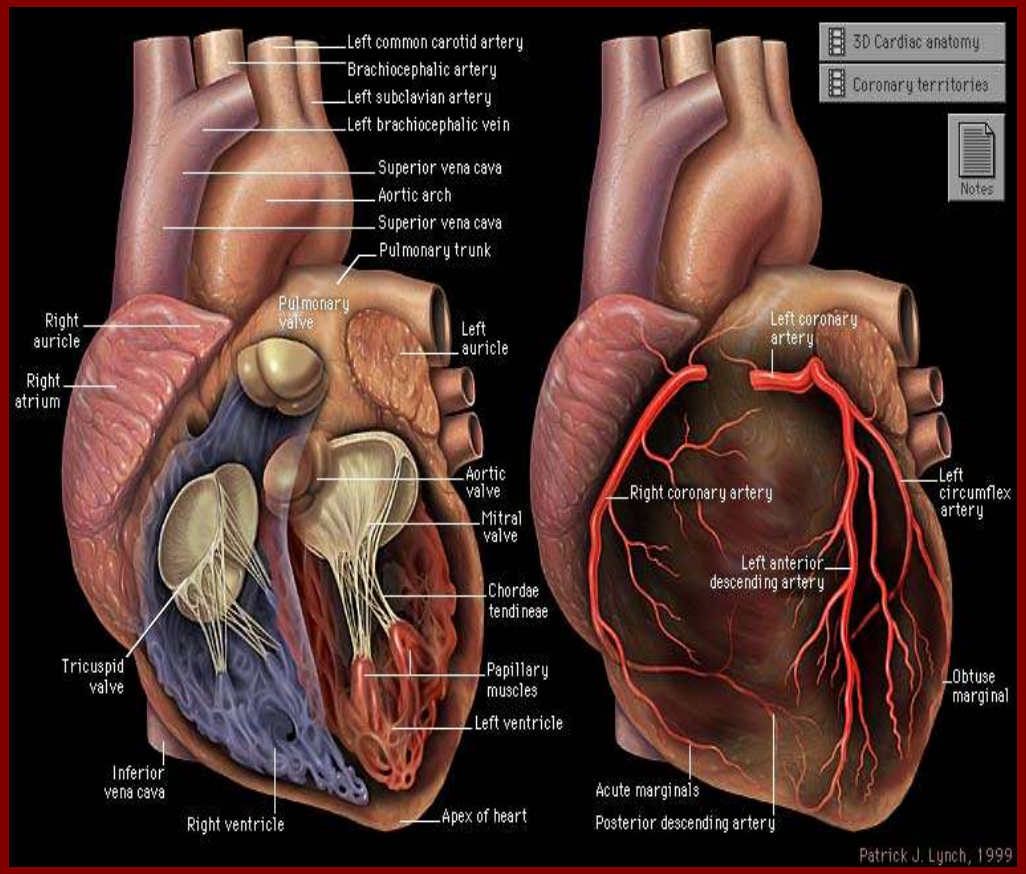
Lupus and Inflammation

- SLE is a chronic, inflammatory disease with circulating **Autoantibodies** (“anti-self”); activated **T cells** (tissue autoimmunity); **immune complexes** (Antigen-Antibody) and inflammatory **Cytokines** (cell messenger proteins)
- Lupus Therapy over the last 4 decades has converted a rapidly fatal disease into a chronic condition

Cardiac Involvement in Lupus

All “layers” of the heart can be involved:

1) Pericardium
2) Myocardium
3) Valves
4) Conducting System
5) Coronary Vessels

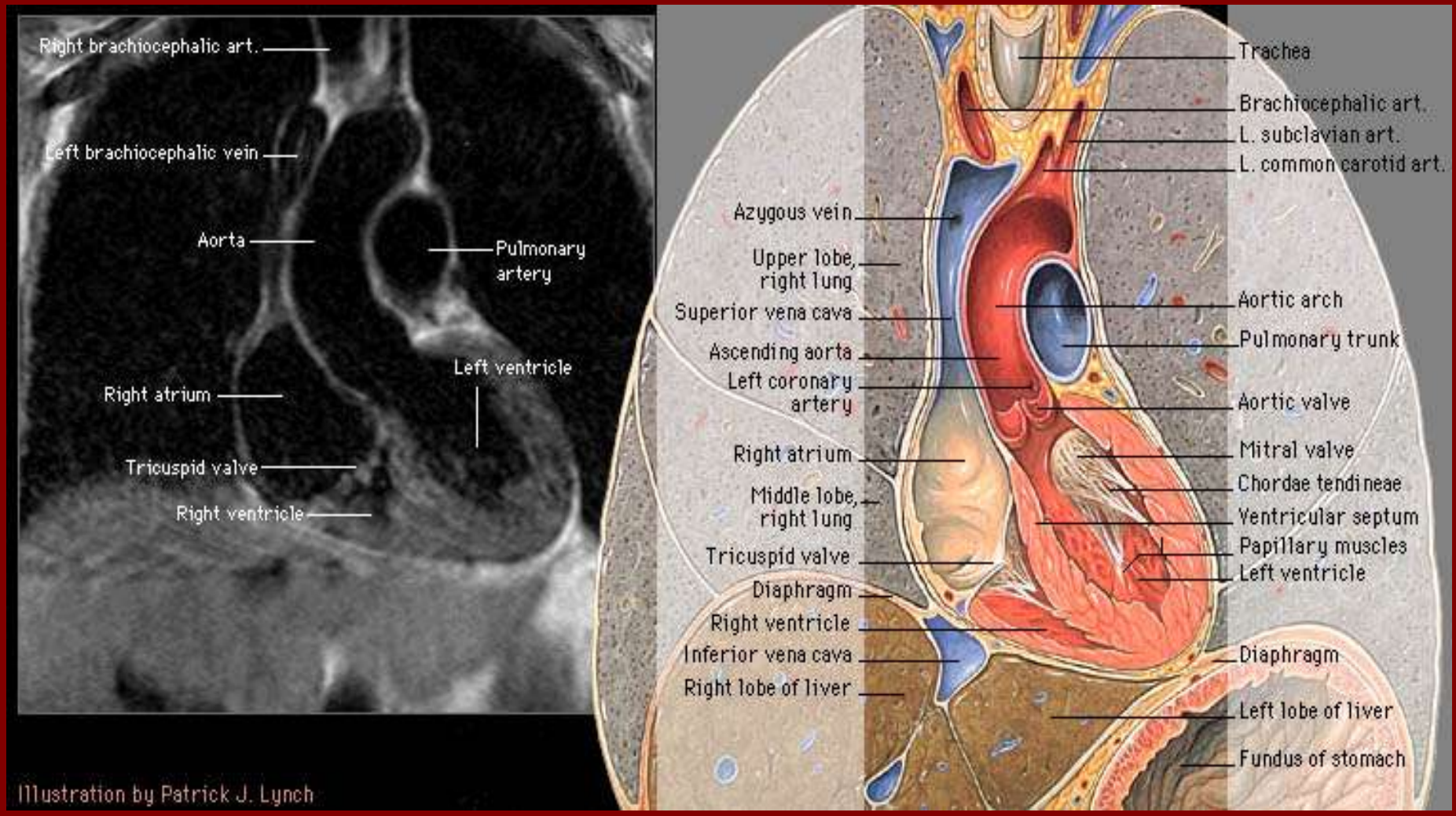


Pericardium

- The thin layer(s) covering the heart
- Inflammation (Pericarditis) occurs in 11-54% of Lupus patients
- Often occurs at Onset or with Relapses
- Pericarditis is the most characteristic feature and is one of the ACR/ARA Classification Criteria for Lupus
- Treated with NSAIDs or Steroids

A. Doria; Lupus; 14; 2005

Pericardium and Pleura

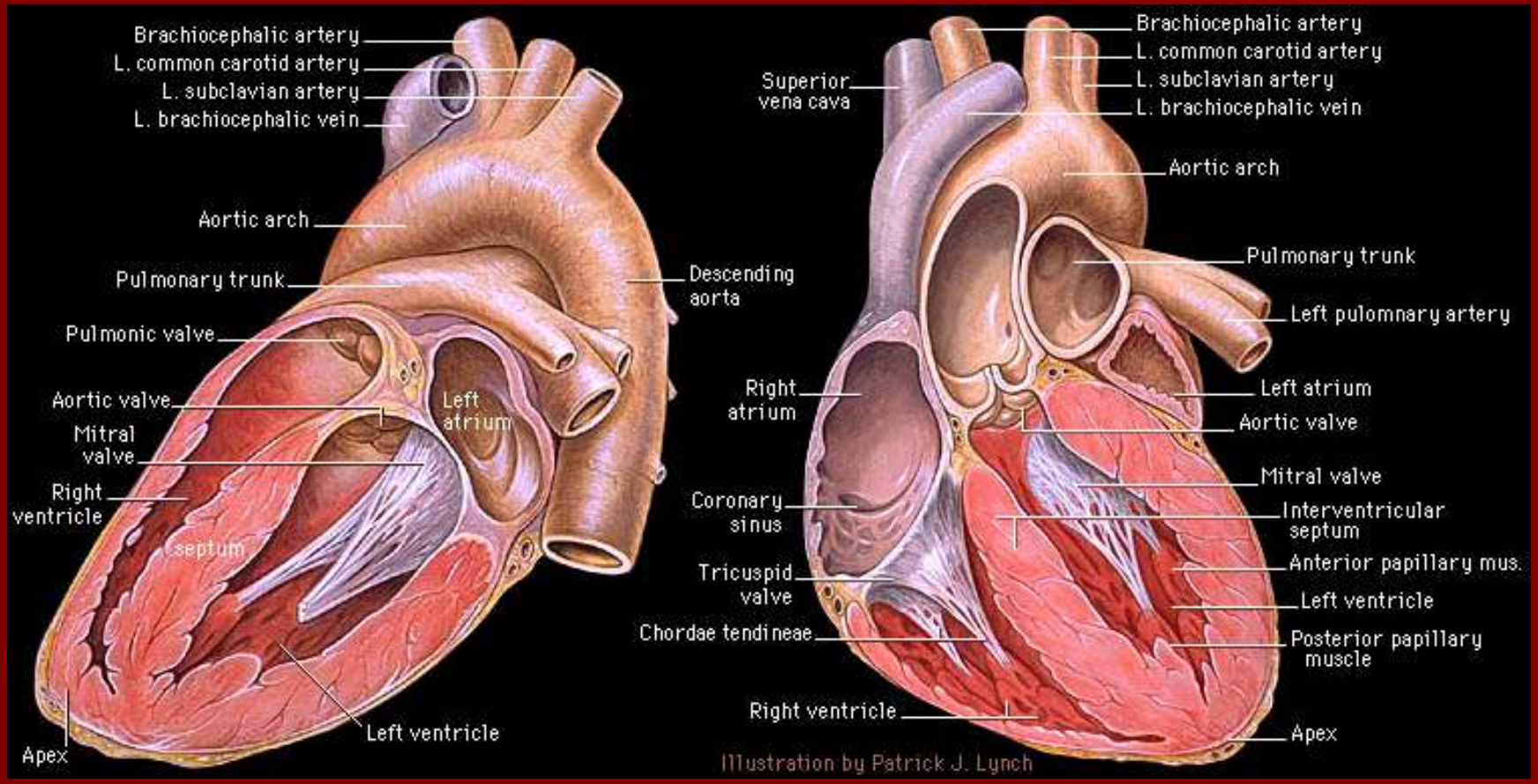


Myocardium

- The active muscle (“pump”) of the heart
- Inflammation (“Myocarditis”) occurs in 7-10% of cases (and is treated with Steroids)
- Myocardial Dysfunction, however, is more commonly due to early coronary artery disease, hypertension, renal failure, valvular disease

Doria; Lupus; 2005

Myocardium and Valves

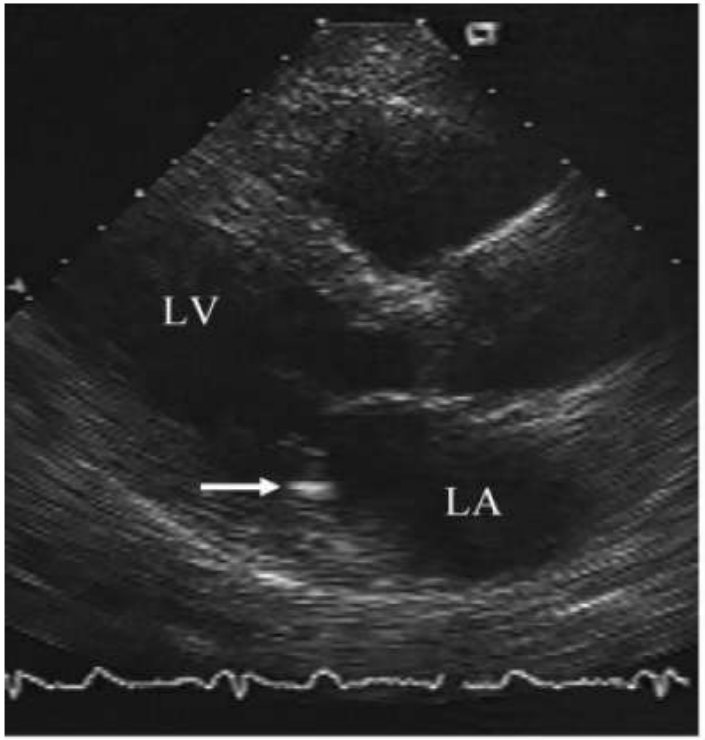


Cardiac Valves

- Connective Tissues that control blood flow into and out of the heart
- Inflammatory lesions usually on Mitral or Aortic Valves (both active and healed)
- Some thickening seen in 40-50% of Echos
- “Verrucous” or Libman-Sacks lesions characteristic but not usual
- Significant clinical valve pathology is unusual (leaking or narrowing)

Doria; Lupus; 2005

Focal Mitral Valve Thickening (51 year-old Lupus patient)



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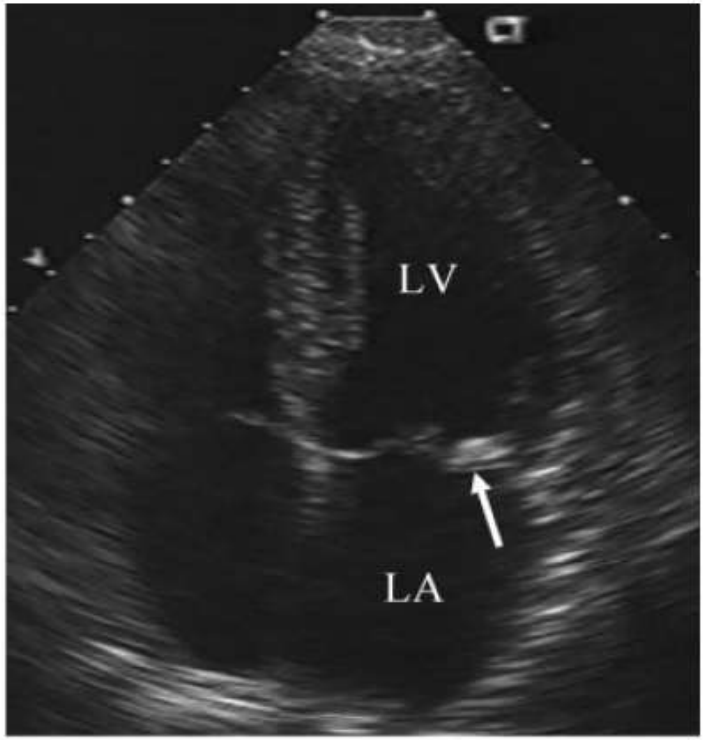


B

Figure 1. Marked focal thickening of the midportion of the posterior mitral valve leaflet (**arrows**) in parasternal long-axis (**A**) and apical 4-chamber (**B**) views in a 51-year-old woman. The lesion is associated with mild mitral regurgitation. **LV** = left ventricle; **LA** = left atrium.

Farzaneh-Far; ArthritisRheum; Dec 2006

Conducting System

- Carries the electrical impulses from the heart's "pacemaker" (Sinus Node) in the atria (top chambers) thru the Atrioventricular Node to the ventricular (pump) muscles (lower chambers)
- Conduction "Block" rare in adults
- Seen in 2% of children born to mothers with Anti-Ro/SSA positive Lupus

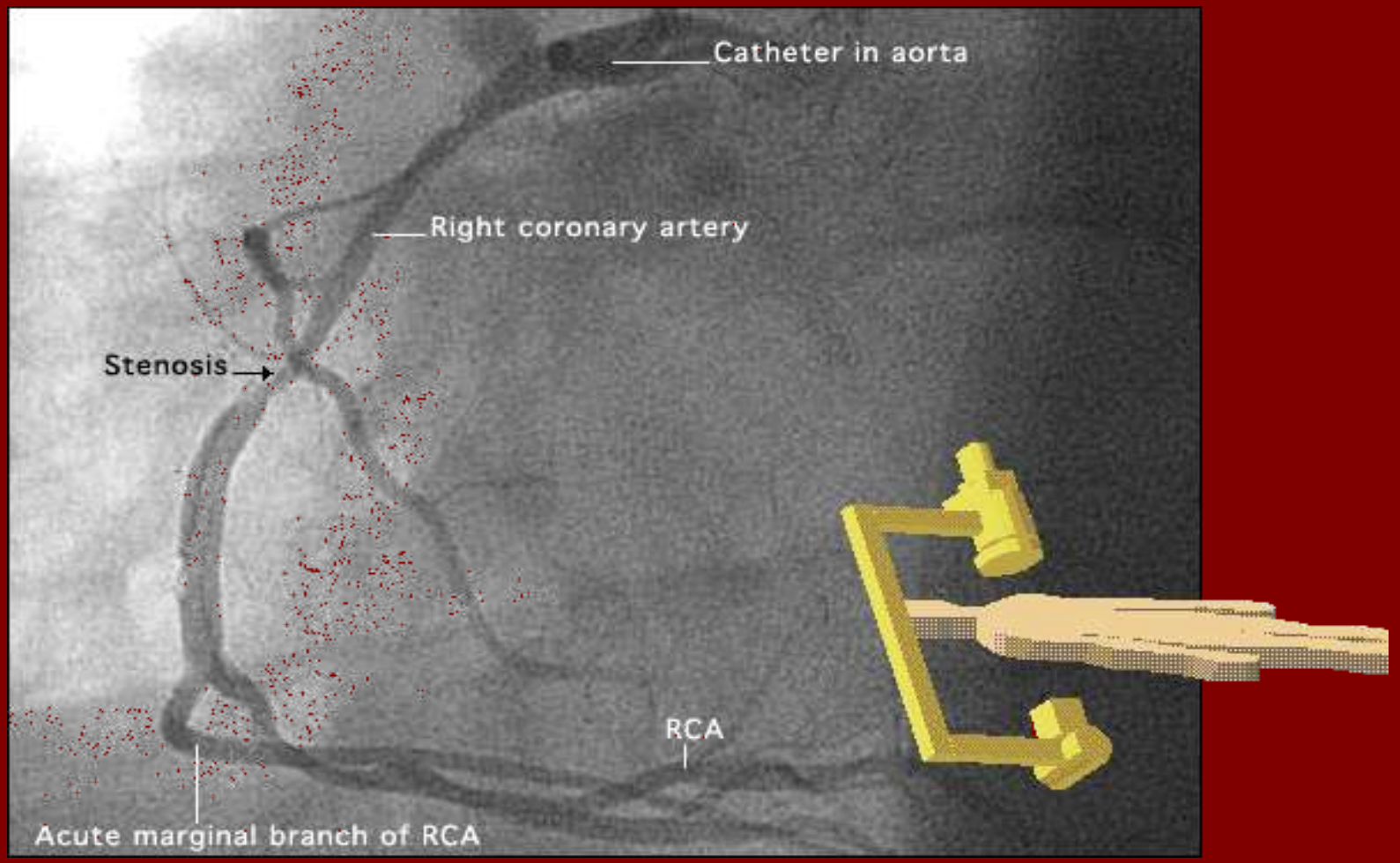
Doria; Lupus; 2005

Coronary Arteries

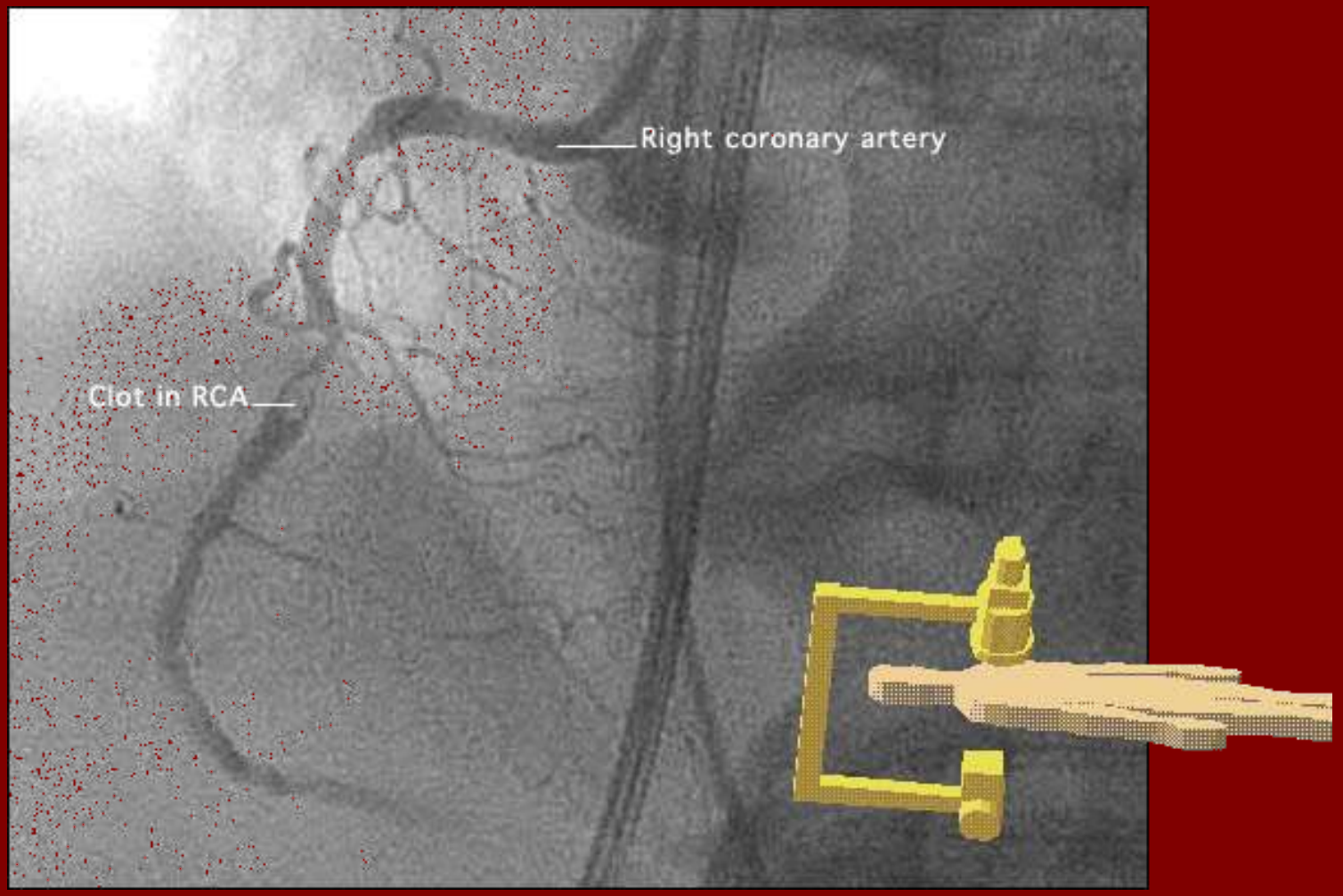
- Larger (surface) and smaller (myocardial) vessels that supply the working muscle of the heart
- Coronary Artery Disease in 6-10%; Lupus patients have a 4-8 fold increased risk of developing CAD
- Smaller vessel inflammation (**vasculitis**)-usually in younger patients with active SLE
- Larger vessel inflammation (**atherosclerosis**)-usually in older patients with long-standing SLE

Doria; Lupus; 2005

Coronary Artery Stenoses (Atherosclerosis)



Acute Coronary Thrombosis



Vascular Disease and Lupus

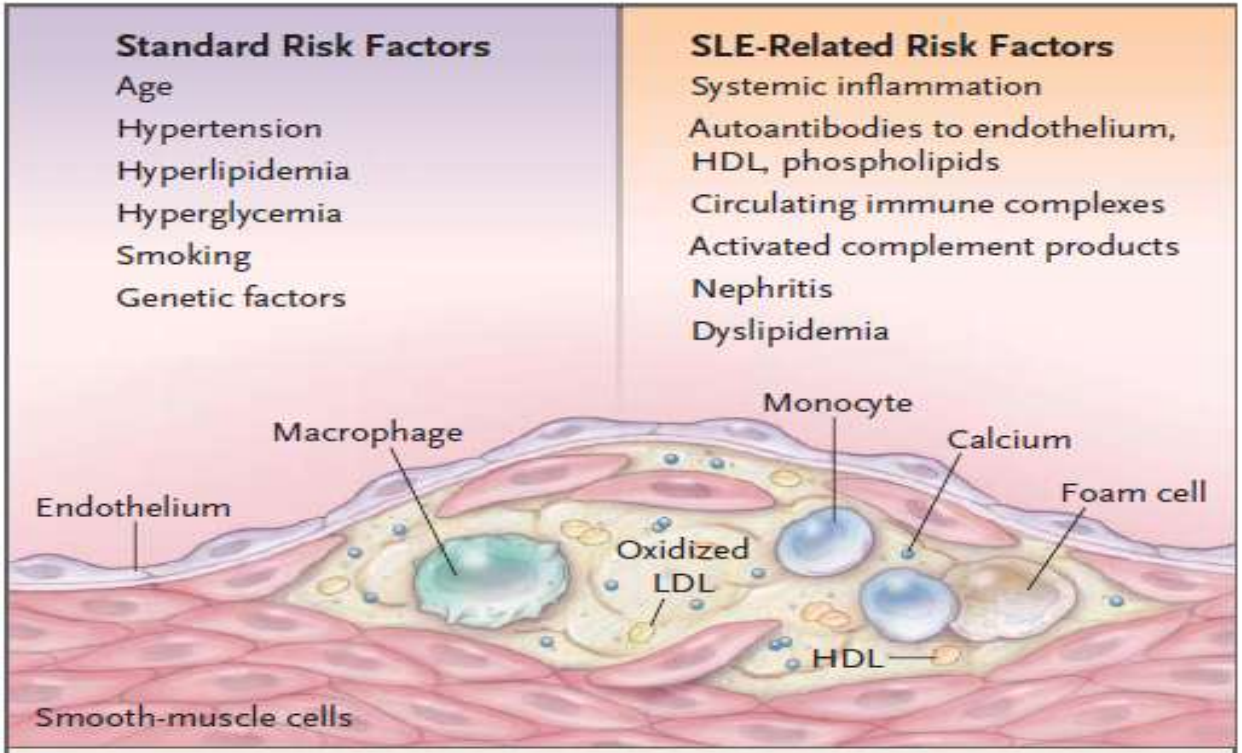


Figure. Risk Factors for Atherosclerosis and Risk Factors Related to Systemic Lupus Erythematosus (SLE).

The figure shows an arterial wall in which plaque and calcification are forming, influenced by multiple factors that accelerate atherosclerosis. LDL denotes low-density lipoprotein, and HDL high-density lipoprotein.

Hahn,B; NEJM; Dec 18, 2003

Inflammation and Vascular Disease

- Atherosclerosis is also a chronic inflammatory disorder, with characteristic **Cellular** (monocyte-macrophage) and **Circulating** (C-reactive protein-"CRP")
- 40% of Lupus patients ages 40-45 have established Carotid Artery Plaque
- Later mortality in SLE is more frequently due to Atherosclerosis—aggressive risk reduction is essential.

Salmon; Curr.Opin.Rheum; 13(5) Sept 2001

Carotid Plaque and Lupus

- Well matched to controls by age, sex, BP and race
- Carotid Ultrasound (focal protrusion > 50% of wall thickness= Plaque)
- Cardiac Echo to examine valve thickening
- Measured hs-CRP and routine serology

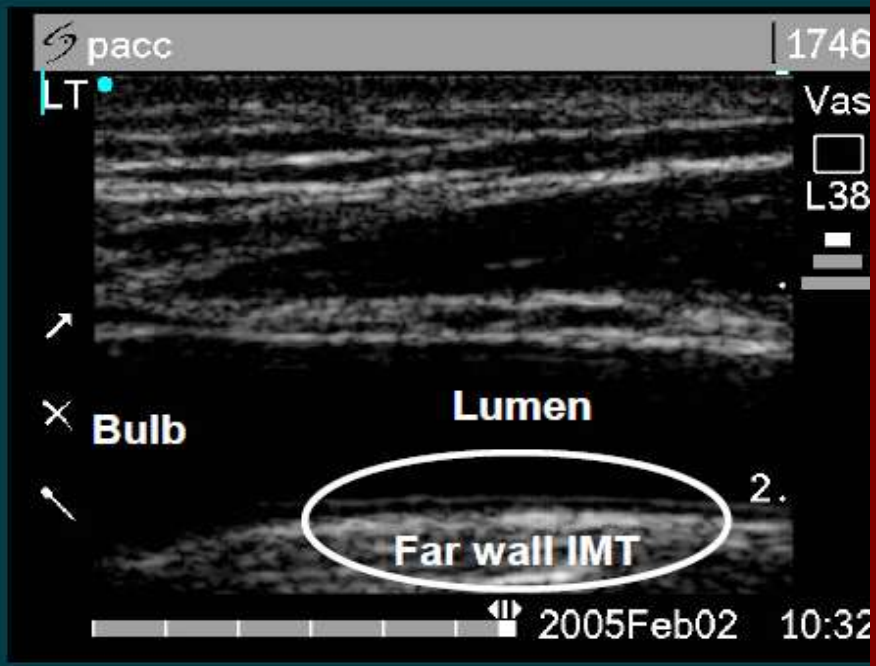
Roman, M: NEJM; 349: Dec 18, 2003

Carotid Ultrasound-I.M.T.

Detection and Measurement

- Far wall
  - Acoustic shadowing in near wall
- Which site?
  - CCA most reproducible
  - ICA/Bulb: more difficult
    - Plaque more common
    - Greater magnitude of change
- Measurement
  - ABD or manual, 1cm length
  - Easy- takes minutes
  - Accurate- .0x mm

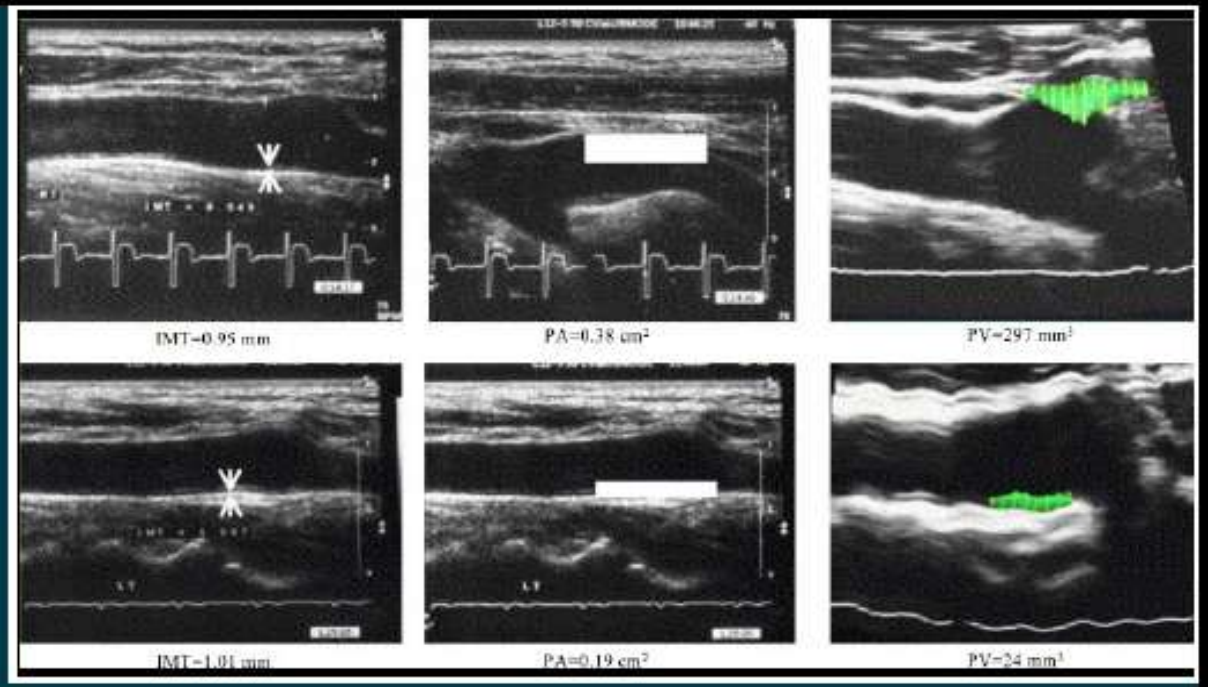
Selection of end-diastolic images
Systolic expansion/IMT thinning



Carotid Ultrasound-Plaque

Dynamic: 3D Carotid Ultrasound Plaque Volume

- Feasible with computer-based reconstruction of US images
- Identifies longitudinal and circumferential changes
- Correlations:
  - IMT-TPA- r = .72
  - IMT-TPV- r = .68



Calcified and Non-Calcified Coronary Plaque

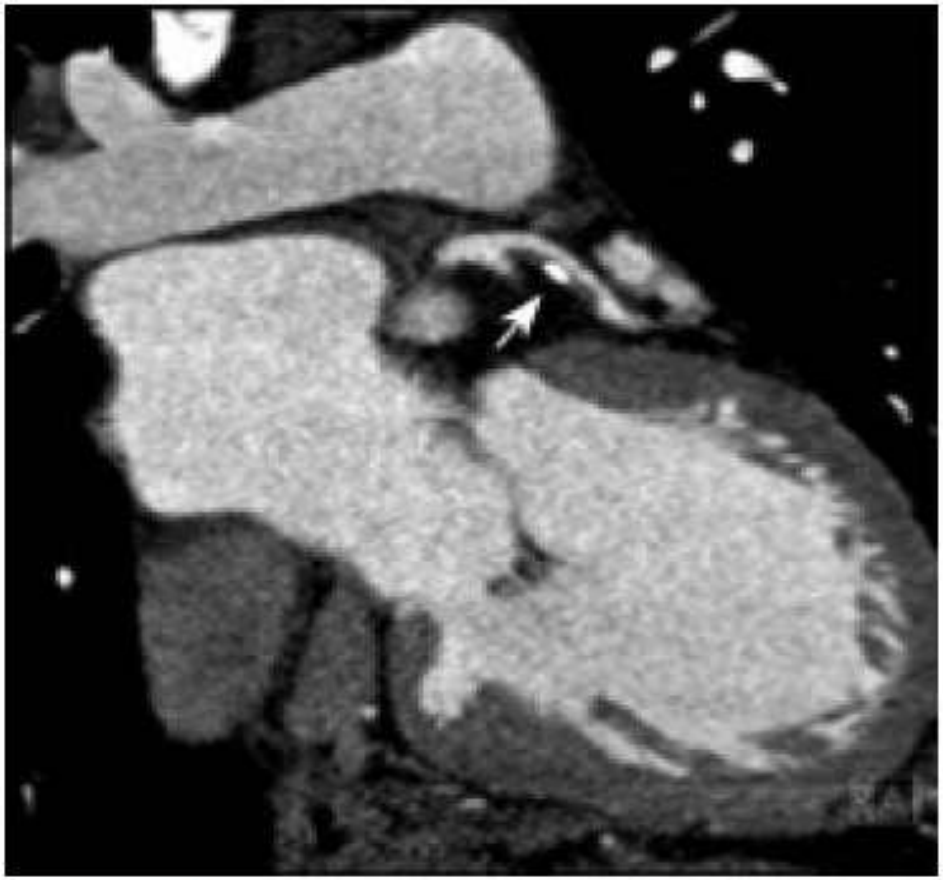


Figure 2. In this multidetector computed tomography scan, the arrow indicates mixed (calcified and noncalcified) plaque.

Kiani, A; J.Rheumatology;37: 579; 2010

Framingham Risk Assessment

- Ongoing study of Cardiovascular Risk in a US cohort; study inception in 1940's
- Allows calculation of Expected 10 year risk of developing Coronary Disease
- Factors in:

Age/Sex

Blood Pressure

Smoking

Cholesterol

Diabetes

LV Hypertrophy

Therapy: Post MI / Post ACS

- A—Aspirin and ACE Inhibitors
- B—Beta Blockers and Blood Pressure
- C—Cholesterol / Cigarettes / Clopidogrel
- D—Diet (for Weight and Diabetes)
- E—Exercise and Education

Conti, CR Clin. Cardiology 2007

Aspirin

- “Class I” for all CAD, MI and PVD patients
- 325 mg/day initially; 81-162mg/d long term
- Post MI: 35 vascular events prevented per 1000 patients x 30d
- 1 life saved at cost of $13 per year!
- ASA allergic?—can use Clopidogrel

Angiotensin Converting Enzyme (ACE) Inhibitors

- For post MI; overt CHF and Heart (LV) dysfunction even without symptoms
- HOPE trial: 25% women; had 22-25% decline in death rates in MI/CAD/Diabetic patients without CHF
- ex: Lisinopril 10-40 mg/d
- If ACE intolerant (allergy or dry cough) use and ARB (ex: Losartan)

Lipid Lowering

- 13-33 death/Mi prevented per 1000 patients x 5 yr
- Measure lipids on initial blood draw
- Start Rx acutely—statins are Anti-Inflammatory (ex: Atorvastatin 10-80/d)
- *Muscle*: usually Myalgias—check CPK; rechallenge or use different statin (pravastatin)
- *Liver*: about 1/1000 asymptomatic mild elevation in liver enzymes

Risk Factors (that modify LDL goal)

- Smoking
- High BP
- Low HDL (< 40)
- Family history CAD
- Central Obesity
- Physical Inactivity
- NOTE: **Diabetes, PVD, Aortic Aneurysm and Coronary Calcium are CHD "Equivalents**"

LDL Goals

Risk Factor	LDL Goal	10 year event rate
CHD or Equivalent	< 100 mg/dl	> 20%
2 or more Risk Factors	< 130 mg/dl	10-20%
0-1 Risk Factors	<160 mg/dl	< 10%

Therapy = “T.L.C.” (Therapeutic Lifestyle Change)

- Decrease Saturated Fat in diet
- Decrease Weight (ideal BMI = 18.5 to 24.9 kg/m2)
- Increase Physical Activity—even walking 30 min day

Lipid Lowering, cont'd

- High Total and LDL Cholest → **Statins**

  High Trig and Low HDL Cholest → **Fibrates**
- High LDL and Trig and low HDL Cholest→ **Niacin** (niaspan)
- High Triglycerides → prescript. **Fish oil** (**Omega 3** FAs)

Diet Modification: Healthy Choices

- Fruits and Vegetables
- Whole Grain and High Fiber
- Oily (cold water) fish 2 x / week
- Alcoholic drink STOP
- Sodium (Na+) < 2.3 gram/day
- Saturated Fat < 10% of total calories

Hormone Therapy

- Estrogen Replacement with or w/o Progestin—of no benefit in preventing CHD
- increased risk of stroke
- Use short term for peri-menopausal Sx only
- Estrogen receptor modulators (raloxifene) of no benefit for CHD.